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ON PLASMA CELLS IN THE TONSILS.*

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The literature on the subject of plasma cells is very extensive and much discussion on the morphology, significance, occurrence, identity, function, etc., of this cell has appeared. Many problems concerning it are unsolved. However, it is generally agreed by most observers, both from experimentation and otherwise, that the plasma cell is a well-defined cell, that it occurs under fairly definite though manifold conditions, and like all other cells is subject to various degenerations, which often give rise to atypical morphological appearances. There are also transitional forms of cells undoubtedly closely related to it. It should be looked on as a cell as clearly defined as, for instance, the polymorphonuclear leukocyte, or the connective tissue cell.

This cell was described definitely first and named by Unna in 1891, and, to be brief, has these characteristics: a roundish oval cell, 6 to 16 μ in diameter, the protoplasm of which stains characteristically by basic dyes (especially pyronin and polychrome methylene blue) and more deeply at the periphery than about the nucleus. Its nucleus is generally eccentrically placed and possesses a characteristic peripheral clumping of chromatin into five to eight definite masses. To these characteristics should be added the presence of the Altmann-Schridde granules in the lighter staining protoplasmic zone immediately about the nucleus.

The origin of these cells has been a much disputed question. Unna thought they came from the connective tissue cells. While this idea is still supported by a few observers, most recent workers now consider them as derived from the small lymphocytes. This view though not original with Schridde has been greatly strengthened if not absolutely proved by his demonstration that the characteristic Altmann-Schridde granules appearing in the protoplasm of plasma cells appear also in the small lymphocytes and in the

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large cells in the centers of lymph follicles. As they are not known to occur in other cells their presence in these three varieties suggest a close relationship. A discussion of the significance of plasma cells will be considered in the latter part of the paper.

This report is based on observations made on about 240 pairs of tonsils; 180 were extirpated chiefly because of hypertrophy, and were mostly from children between five and 15 years. There were many, however, from young adults who had suffered from recurrent tonsilitis, rheumatism, nephritis, etc. The remainder, about 60 in number, were obtained at autopsies from subjects of various ages, ranging from the fetus to the very aged;[1] seventeen were infants less than three months old. With few exceptions the tonsils from autopsies appeared normal. As a routine method of staining the methyl-green-pyronin stain of Pappenheim was used.

Concerning the occurrence of plasma cells in the tonsils the following facts were noted: They are not found in the fetus or in the newborn child. They make their appearance in the tonsils with more or less regularity about the second and third week of life. Some variability in this respect exists. In one case, for instance, during the second week a few were found; in another case, at the end of the third week none was found; in still another, at the end of the eighth week none was found. In no case examined older than this were they absent. At first very few are found and they are seen as a rule just beneath the epithelium lining the crypts. They increase in number gradually, so that in children several months old they occur as a rule constantly and abundantly. They remain present throughout life, even to very old age (88 years the oldest examined), regardless of the anatomic condition of the tonsil. In pathological tonsils, and especially in hypertrophy, they are far more numerous.

As to their distribution in the tonsil, they occur chiefly in three localities. They are most numerous just beneath the epithelium, especially that lining the crypts. In the papillae they are often seen in large numbers about the small blood vessels.

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[1] Much of this postmortem material was obtained at the Pathological Institute at Freiburg i. Br. Director Professor Aschoff, to whom I wish here to acknowledge my indebtedness for many favors.

Beneath the surface epithelium they are found, but generally not in abundance. Often in the epithelial layers they may be seen in the act of migration, and when thus found are usually single or in twos. They may be free in the crypts but as a rule in very small numbers.[1] A second locality where they are found abundantly is along and in the meshes of the connective tissue that surrounds and penetrates the tonsil. Here they occur singly or in loose clusters and are often associated with mast cells, which are always far less abundant. Thirdly, they often but by no means always may be seen clustered about the smaller blood vessels at various depths in the lymphoid tissue. In addition to these localities occasional plasma cells may be seen in the lymphoid tissues, though it is somewhat surprising how rare they are here. It is possible, of course, that such isolated cells may be near a small blood vessel located outside the section. I have never in any case observed a typical plasma cell in the center of a lymph follicle. They often occupy lymph spaces, especially the perivascular lymphatics though they are not limited to such vessels. Apparently they wander through the various tissues as they do through the epithelium into the crypts. In hypertrophied tonsils their distribution is not different from that in normal tonsils. As was stated, they are more numerous and I think their number is roughly proportional, in a general way, to the increase in size. In such cases they are seen in clusters or often in a continuous layer under the epithelium or about blood vessels. A not inconsiderable part of the increase in size of such tonsils is evidently due to the accumulation of the plasma cells.

In connection with the facts concerning the time of the appearance of plasma cells in tonsils I made some observations with the view of determining at what time the tonsillar crypts are invaded by bacteria. As is well known, tonsils from the fetus and newborn are sterile. Cultures made during the first week and later reveal bacteria, as do also stained preparations of the tonsils. These bacteria are a mixture of various bacilli and pyogenic cocci. Evi-

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[1] It should be stated that plasma cell-emigration seen in the epithelium of the tonsils is entirely different from the lymphocyte-emigration described years ago by Stöhr, who thought the lymphocytes passed through the epithelium, leaving openings (physiological wounds) through which bacteria might enter.

A careful and systematic study of these cells has apparently not been made in the tissue of the fetus and the newborn. Schridde[1] states that only in later life are plasma cells found in the spleen and are to be regarded as pathological. Aschoff has observed that in the appendix in the newborn, plasma cells are not present. Soon after birth they appear and are thereafter found constantly in all appendices, normal and pathological. In lymph glands they occur commonly, especially in glands undergoing fibrosis. I have seen them in enlarged glands in Hodgkin's disease but not in large numbers. I can find no statement concerning their occurrence in lymph glands of the fetus or newborn. Such glands examined by me in a few cases, revealed no plasma cells. Porcile[2] observed plasma cells in the livers of two newborn children, one having syphilis of the liver, the other syphilis of the lung.

In general, then, these cells may be said to occur chiefly in chronic inflammatory lesions, along the gastro-intestinal canal and in connection with certain atrophic processes. Now in view of the fact that plasma cells occur in such large numbers in tonsils, appendix, and some other tissues after birth at a time when the crypts and intestinal canal are infected, and associating this with the fact that in chronic infections generally the plasma cell is so constantly found, one is led to suggest that their presence in the tonsil and appendix, and also in the gastro-intestinal tract, lymph glands, and spleen is due to a chronic infectious or absorptive process. In such organs as the tonsil and the appendix, whose crypts or lumen are constantly infected by many organisms, often, as has been shown, of a pathogenic nature, absorption of bacteria or toxic products must occur to some extent. This is also true throughout the intestinal canal, as it is well known that bacteria are constantly passing through the wall into the lymphatics and blood stream. Indeed, Dantchakow and Pirone,[3] after noting the occurrence of these cells especially in the intestinal mucosa in atrophic organs like the thymus and following the injection of tissue extracts, suggested that the absorption of ferments caused sufficient irritation dently, then, as one would expect, invasion of the tonsillar crypts occurs at about the same time as, or shortly after, the intestinal canal is invaded by bacteria, which is, as has been shown by others, from 24 to 72 hours after birth.

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[1] *Pathologische Anatomie, L. Aschoff.*, 2, p. 116.

[2] *Beitr. z. path. Anat. u. z. allg. Path.*, 1904, 36, p. 375.

[3] *Centralbl. f. allg. Path. u. path. Anat.*, 1909, 20, p. 1011.

It thus appears that soon after invasion of the tonsils by bacteria the plasma cells appear in these organs. The question at once arises as to whether these two phenomena are in any way related and whether the one is dependent on the other. This problem perhaps can not be decided definitely, but it may be worth while to make a few statements which may have some bearing on this point.

Plasma cells are found chiefly in connection with pathological lesions, especially those of a chronic nature (granulomats). In acute infections they are not numerous. But in chronic infections they are present, usually in enormous numbers, and in certain conditions, as, for example, in gonorrheal salpingitis, their numbers and location may be sufficiently characteristic to be of aid in diagnosis (Schridde, Amersbach). In some skin disceases, as in lupus, mycosis fungoides, and some others, they accumulate in large masses in the lesions. They are known to occur constantly in the gastrointestinal mucosa, and J. Schaffer[1] has observed them in the involuting thymus in man, the mole, mouse, dog, and white rat. They are found commonly in tumors, especially at the margin of carcinomats. Tumors have been described (Wright, Aschoff, Hoffmann, Christian), occurring chiefly in the bone marrow, which are composed almost entirely of plasma cells (plasmocytoma). These tumors do not produce metastases, and therefore by some are considered in the group of chronic infectious granulomats.

Experimentally it has been shown by a number of observers[2] that extensive accumulations of plasma cells occur in animals following the injection of various bacteria. This is true especially for Friedländer's bacillus and the gonococcus. The introduction subcutaneously or intraperitoneally of irritating nonbacterial substances, such as turpentine and tissue extracts, also gives rise to an accumulation of these cells.

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[1] *Centralbl. f. Phys.*, 1909, 22, p. 858.

[2] *Centralbl. f. allg. Path. u. path. Anat.*, 1909, 20, p. 1011.

to promote the accumulation of plasma cells. This may be entirely or only partially true.

In the case of the tonsil, however, the view is more rational that this organ is, in all cases, whether hypertrophied or not, a chronically infected focus from a time shortly after birth, a view apparently supported by bacteriological studies. It therefore seems reasonable that cells more or less characteristic of chronic inflammation should accumulate here. Not only the nature of these cells, moreover, but their accumulation in such large numbers and in localities immediately underneath the epithelium, especially about the infected crypts, also favors such a view. Similar conditions evidently exist in the appendix, another organ which is so often subject to severe infections.

SUMMARY.

In the tonsils of the fetus and the newborn, plasma cells are not present. They first appear about the second or third week, and thereafter are constantly found in the tonsils. This is about the time, or shortly after the time, that bacteria invade the tonsillar crypts. In hypertrophied tonsils they are more numerous than in apparently normal tonsils. Their presence may be interpreted as indicating the existence in the tonsils of a chronic infectious process or the absorption of toxic or irritating products.